

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



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Applicant's or agent's file reference 4-32342A	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP03/00954	International filing date (day/month/year) 30.01.2003	Priority date (day/month/year) 31.01.2002
International Patent Classification (IPC) or both national classification and IPC C07D215/14		
Applicant NOVARTIS AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 26.07.2003	Date of completion of this report 06.10.2003
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Stix-Malaun, E Telephone No. +49 89 2399-8057 

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International application No. **PCT/EP03/00954**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-42 as originally filed

Claims, Numbers

1-5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-5
	No: Claims	
Inventive step (IS)	Yes: Claims	1-5
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-5
	No: Claims	

2. Citations and explanations

see separate sheet

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report

- D1: US-A-5 049 577 (R.K. VARMA ET AL) 17 September 1991 (1991-09-17)
D2: P.D. THEISEN ET AL: J. ORG. CHEM., vol. 53, no. 10, 1988, pages 2374-2378, XP002218099
D3: EP-A-0 340 007 (E.R. SQUIBB & SONS INC) 2 November 1989 (1989-11-02)
D4: US-A-5 034 399 (W. HÜBSCH ET AL) 23 July 1991 (1991-07-23)
D5: US-A-5 354 772 (F.G. KATHAWALA) 11 October 1994 (1994-10-11)
D6: US-A-5 856 336 (Y. FUJIKAWA ET AL) 5 January 1999 (1999-01-05) cited in the application

have been considered for the examination procedure.

2. NOVELTY

The claimed subject-matter is considered to be novel (Article 33(2) PCT):
The essential procedural difference between the claimed compounds and those of D1-D6 lies in the fact that a chiral phosphonate derivative containing an amid group is used in the Wittig-Wadsworth-Emmons reaction.

3. INVENTIVE STEP

The Claims appear to fulfil the requirements of Article 33(3) PCT:
The problem of the present application may be seen in the provision of an enantioselective process for the preparation of polyhydroxy derivatives being economically attractive, e.g. by using less reaction steps (see description, p. 5, third paragraph).

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The closest state of the art for the present application is represented by D1.

D1 discloses a similar process for the preparation of HMG-CoA Reductase inhibitors falling under present formula (I). Similar to present claim 1 the compounds of D1 are prepared by using a chiral phosphonate derivative as the reagent for the Wittig-Wadsworth-Emmons reaction. Said phosphonate differs in the fact that it contains an ester instead of an amid functionality. In other words the presently claimed subject matter is simplified by omitting the transformation from the amid to the ester.

This simplification is neither from D1 alone nor from the combination with D2-D6 derivable. Therefore the application involves an inventive step.-